REMARKS

Applicants thank the Examiner for examination of Claims 1-8 and 22-25 of Groups I and II. Applicants also thank the Examiner for consideration of the references listed on the Information Disclosure Statement dated March 14, 2006. In the instant Office Action the Examiner raised several issues, which are set forth by number in the order they are addressed herein:

1) Claim 1 is objected to as allegedly being informal;
2) Claims 1-8 and 22-25 stand rejection under 35 USC § 112, first paragraph, as allegedly lacking enablement;
3) Claims 1-8 and 22-25 stand rejected under 35 USC § 112, second paragraph, as allegedly being indefinite;
4) Claims 1, 5, 6 and 22-24 stand rejected under 35 USC § 102(b), as allegedly anticipated by Freedman et al., Proc Natl Acad Sci USA, 94:587-592, 1997 (Freedman); and
5) Claims 2-6, 23 and 24 stand rejected under 35 USC § 102(a), as allegedly anticipated by Leonard et al., Arch Gen Psych, 59:1085-1096, 2002 (Leonard).

Applicants hereby amend Claims 1, 2 and 7, cancel Claims 3, 4 and 9-25, and introduce new Claims 26-37, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments. Applicants reserve the right to prosecute the original, similar, or broader claims in one or more future application(s). The amendments do not introduce new matter.

1) Claim 1 is Proper

The Examiner has objected to Claim 1 as allegedly being informal for lacking the word "to" between the terms "predisposed" and "schizophrenia." Applicants thank the Examiner for drawing this clerical error to their attention. Accordingly Applicants have amended Claim 1 to recite "predisposed to schizophrenia."

2) The Claims Are Enabled

The Examiner has rejected Claims 1-8 and 22-25 under 35 USC § 112, first paragraph, as allegedly lacking enablement. In particular the Examiner has stated that there is "no way to genetically diagnose schizophrenia" and that the "art does not teach all variants of the alpha-7 nicotinic receptor allele and does not teach that every allelic variant or polymorphism is related to schizophrenia" (Office Action, page 4). Applicants respectfully disagree that the claims lack enablement.

Nonetheless Applicants have amended Claims 1, 2 and 7, canceled Claims 3, 4 and 9-25, and introduced new Claims 26-37 in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, and while reserving the right to prosecute the original, similar, or broader claims in one or more future application(s). In particular, Applicants have amended Claim 1 to recite "wherein said at least one polymorphism contributes to reduced transcription," and have amended Claim 2 to recite specific polymorphisms for which evidence of reduced promoter activity has been provided. Support for the amendment of Claim 1 can be found for instance in original Claim 4, now canceled. Further support for the amendments to Claims 1 and 2 can be found but is not limited to Example 15 and Figure 13, which disclose methods for assessing promoter activity of various α7 variants, and results so obtained. In addition Applicants have introduced new Claims 26-37 which are directed to identifying individuals predisposed to schizophrenia by detecting at least one of multiple α7 polymorphisms found more frequently in schizophrenic individuals than in normal controls. Support for new Claims 26-37 can be found in original Claims 1-8. Further support for Claims 26-37 can be found but is not limited to Example 13 including Table 7. Thus pending Claims 1, 2, 5, 6 and 26-37 are directed to α7 alleles having a promoter polymorphism associated with reduced activity and/or to discreet allelic variants or polymorphisms found significantly more often in schizophrenics than in controls.

Applicants respectfully point out that pending Claims 1, 2, 5, 6 and 26-35 do not require the step of "providing a diagnosis." In addition, Applicants have amended Claim 7, and have introduced new Claim 36, which recite "step d) providing a diagnosis of schizophrenia to said subject based on the presence of said at least one polymorphism and a physician interview."

Support for this amendment is found, for instance, in Example 17, which discloses the analysis of medical records and the use of physician interviews for diagnosis of schizophrenia.

As the pending claims are enabled, Applicants respectfully request that this rejection be withdrawn.

3) The Claims Are Definite

The Examiner has rejected Claims 1-8 and 22-25 under 35 USC § 112, second paragraph, as allegedly being indefinite. The Examiner has rejected Claims 1-3 and 22 as allegedly vague "in so far as they employ terms such as 'α7 allele' or -241 A to G' as limitations without reference to precise nucleic acid sequences. The Examiner has also rejected Claims 7, 8 (and 25) as allegedly indefinite because "it is not clear what they diagnose" and because the method "cannot simultaneously indicate a predisposition and indicate a diagnosis of the disease." The Examiner has further rejected Claims 1 and 22 as allegedly incomplete for "omitting essentials steps" such as "wherein the conditions for identifying are either met or not" (Office action, pages 5 and 6). Applicants respectfully disagree that the claims are indefinite.

Nonetheless, Applicants have amended Claims 1, 2 and 7, canceled Claims 3, 4 and 9-25, and introduced new Claims 26-37 in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, and while reserving the right to prosecute the original, similar, or broader claims in one or more future application(s). In particular Applicants have amended Claim 1 to recite "detecting the presence of at least one polymorphism within a core promoter region corresponding to SEQ ID NO:125 of said α7 allele." Moreover, Applicants have amended Claim 2 and introduced new Claim 26, which recite "in relation to a start codon of said α7 allele beginning at residue 270 of SEQ ID NO:125." Support for these amendments can be found for example in Figure 12B showing the core promoter region for the CHRNA7 gene set forth as SEQ ID NO:125, with arrows depicting the locations of polymorphisms identified during development of the present invention.

Furthermore as discussed above in Section 2, Applicants have amended Claim 7 and have introduced new Claim 36, which recite "step d) providing a diagnosis of schizophrenia to said subject based on the presence of said at least one polymorphism and a physician interview." Thus, the methods of Claims 7, 8, 36 and 37 are directed to the diagnosis of schizophrenia.

Lastly, Applicants contend that step c of Claims 1 and 26 which recites "correlating the presence of said at least one polymorphism with a predisposition to schizophrenia" in connection with amended or new step b reciting α7 polymorphisms associated with schizophrenia, are suitable final steps. Thus the methods of Claims 1 and 26 clearly provide condition(s) for identifying individuals and a criterion for determining whether these conditions have been met (e.g., presence of at least one α7 promoter polymorphism).

As the pending claims are definite, Applicants respectfully request that this rejection be withdrawn.

4) The Claims Are Novel Over Freedman

The Examiner has rejected Claims 1, 5, 6 and 22-24 under 35 USC § 102(b), as allegedly anticipated by Freedman et al., Proc Natl Acad Sci USA, 94:587-592, 1997 (Freedman). The Examiner states that

> Freedman et al recite providing nucleic acids from control and schizophrenic subjects (see methods, page 588) to link a polymorphism (S15S1360) near exon 2 in the alpha-7 allele and a high P50 ratio, which is an auditory deficit, linked to schizophrenia (Office Action, pages 6 and 7).

Applicants respectfully disagree with this rejection. Even so, as described above in Sections 2 and 3, Applicants have canceled Claims 22-24, amended Claim 1 and introduced new Claim 26, which are directed to polymorphisms in the core promoter region of an α7 allele. As Freedman does not teach the polymorphisms of the pending claims, Freedman does not anticipate the claims. Accordingly, Applicants respectfully request that this rejection be withdrawn.

5) Leonard Is Not Prior Art

The Examiner has rejected Claims 2-6 and 23-24 under 35 USC § 102(a), as allegedly anticipated by Leonard et al., Arch Gen Psych, 59:1085-1096, 2002 (Leonard). The Examiner states that

> Leonard et al describe a method comprising obtaining a sample comprising the alpha7 allele from postmortem brain (page 1087), detecting the presence of at least one polymorphism by sequencing (see methods, page 1085), and correlating

the presence of said at least one polymorphism with a predisposition to schizophrenia (Office Action, page 7).

"The Leonard Declaration" (attached hereto at Tab 1) is provided as evidence that the Leonard publication describes Applicants work. Since Leonard is not prior art, Applicants respectfully submit that this reference does not anticipate (or make obvious) the pending claims.

CONCLUSION

Applicants believe the amendments and arguments set forth above traverse the Examiner's rejections and, therefore request that a timely Notice of Allowance be issued in this case. However, should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect.

Dated: December 6, 2006 By: 

Christine A. Lekutis
Registration No. 51,934

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
415.904.6500